REMARKS

Claims 113-119 are pending in this application. Claims 1-112 and 120-133 are withdrawn by the examiner. Applicants cancel claims 1-112 and 120-133 without prejudice or disclaimer. Claims 113-119 are amended to correct informalities and for clarity. The term "injectable hydrogel" added to the claims is supported by the specification (see for example, page 5, lines 22-26; page 54, lines 4-17). Other amendments to the claims also are fully supported by the specification as indicated below. Therefore, no new matter has been introduced. The Office Action is discussed below:

Election/Restriction:

Claims 113-119 (Group II) have been elected. Claims 1-112 and 120-133 are withdrawn by the examiner. In order to expedite the prosecution, applicants cancel claims 1-112 and 120-133 without prejudice or disclaimer. However, applicants reserve the right to pursue the cancelled claims in one or more divisional applications.

Indefiniteness Rejection:

On pages 2-3 of the Office Action, the examiner has rejected claims 114-119 allegedly as being indefinite and asserted that it is not clear if the "weight percent" is the concentration of the PVA in the solution, the concentration of the PVA in the hydrogel or if it is the concentration of PVA solution. In response, applicants clarify that it is the concentration of the PVA solution. Applicants refer to the specification for further clarification of the term "weight percent polyvinyl alcohol" (see for example, page 28, lines 13-15; page 31, lines 4-8; page 38, lines 10-12; and page 62, lines 27-29).

The examiner also alleges that the claims are unclear in distinguishing PVA solution and the composition of the hydrogel. In response, applicants refer to above clarification of the "weight percent polyvinyl alcohol" and for additional clarity, further amend claim 114 to recite that "the hydrogel composition is prepared by mixing at least about 1.0 weight percent polyvinyl alcohol with a solution of about 1.5 to about 6.0

molar sodium chloride." The amendment is fully supported by the specification, see for example, page 28, lines 13-15, and page 31, lines 4-8 for a description of the "weight percent polyvinyl alcohol"; and page 7, lines 25-28, page 82, lines 10-11, original claim 110, and page 11, lines 24-27, for molar concentration of sodium chloride.

Withdrawal of the indefiniteness rejection is therefore solicited.

Anticipation/Obviousness Rejection:

On page 3 of the Office Action, the examiner has rejected claim 113 allegedly as being anticipated by Hyon (US 4,663,358), Ottoboni (US 5,731,005), Tanihara (US 5,880,216), KU (US 5,981,826), Yao (US 6,268,405), Yamauchi (JP 03215417), or Okamura (JP 04338326). According to the examiner, both Hyon and Yamauchi individually disclose PVA hydrogels while others disclose PVA hydrogels in NaCl solutions. Applicants respectfully disagree with the examiner and point out that none of the cited references disclose the claimed cross-linked hydrogel composition, which is substantially free of chemical cross-linkers.

On page 4 of the Office Action, the examiner has rejected claims 114-119 allegedly as being anticipated by or, in the alternative, as being obvious over Ottoboni (US 5,731,005), Tanihara (US 5,880,216), KU (US 5,981,826), Yao (US 6,268,405), or Okamura (JP 04338326). Again, applicants respectfully disagree with the examiner and point out that none of the cited references or any combination thereof disclose the claimed hydrogel composition comprising a physically cross-linked polyvinyl alcohol.

Applicants note that in order to reject a claim under 35 USC § 102, the examiner must demonstrate that each and every claim term is contained in a single prior art reference. *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 18 USPQ2d 1001, 1010 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 90 (Fed. Cir. 1986); *see also* MPEP § 2131 (Rev. 3, August 2005). Claim terms are to be given their plain meaning as understood by the person of ordinary skill in the art, particularly given the limitations of the English language. *See* MPEP § 2111.01 (Rev. 3, August 2005). Claims are to be given their broadest reasonable interpretation

consistent with applicants' specification. *See In re Zletz*, 13 USPQ2d 1320, 1322 (Fed Cir. 1989) (holding that claims must be interpreted as broadly as their terms reasonably allow); see MPEP § 2111 (Rev. 3, August 2005).

Not only must the claim terms, as reasonably interpreted, be present, an allegedly anticipatory reference must enable the person of ordinary skill to practice the invention as claimed. Otherwise, the invention cannot be said to have been already within the public's possession, which is required for anticipation. *See Akzo, N.V. v. U.S.I.T.C.*, 1 USPQ2d 1241, 1245 (Fed. Cir. 1986).

Applicants provide the following explanations in order to assist the examiner in distinguishing the cited arts from the claimed invention and submit that:

Hyon *et al.* (US 4,663,358) describe a method for preparing a PVA-based hydrogel through a freeze-thaw process. Freeze-thaw process does not permit preparation of an injectable formulation. Hence, Hyon method can not yield an injectable hydrogel. Therefore, Hyon does not anticipate the claimed invention.

Ottoboni *et al.* (US 5,731,005) discuss a method of making hydrogel microspheres through the use of chemical cross-linkers. Ottoboni *et al.* do not describe physical cross-linking of PVA, nor do they contemplate an injectable pre-hydrogel solution that gels *in situ* without chemical cross-linkers. Therefore, Ottoboni can not anticipate the claimed invention.

Tanihara *et al.* (US 5,880,216) describe about chemical modifications to the PVA repeat unit to improve heat resistance and the resulting material is no longer PVA. Although Tanihara mentions about salts, the hydrogels do not contain salt. Applicants note that the salt is not included as a gellant (see col. 2, lines 25-28) and does not operate as a gellant, but rather has either therapeutic qualities or is a solid entrainment to increase the modulus of the hydrogel. The remainder of the Tanihara disclosure does not mention salt (see for example, specifically col. 3, lines 42-45, col. 20, lines 28-40). Moreover, Tanihara gel is not injectable. Therefore, Tanihara does not anticipate the claimed invention.

Ku *et al.* (US 5,981,826) teaches the process of forming hydrogels from PVA by a freeze-thaw process and the resultant hydrogels are 'cryogels'. This is a similar process as described by Hyon *et al.* (see above). The salt content used by Ku (see for example, col. 4, lines 36-39), which is 0.9 wt.%, or isotonic saline, can not form a hydrogel according to the claimed invention. As with Hyon, Ku's process also does not result in a hydrogel pre-cursor solution that will ultimately gel without freezing. As noted above, a freeze-thaw process does not permit preparation of an injectable formulation. Hence, Ku method can not yield an injectable hydrogel composition according to the claimed invention. Therefore, Ku does not anticipate the claimed invention.

Yao *et al.* (US 6,268,405) also disclose a process of forming hydrogels from PVA by a freeze-thaw process (see for example, col. 3, lines 13-14). Yao suggested to add iron and magnesium salts to prevent calcification of the cryogel while it is inside the body. In the Yao process, salt is added as a solid, which creates pores in the cryogel. After gelation, the salt particles are washed away, leaving behind a sponge (see for example, col. 13, example 3). Yao demonstrates in example 3 that just adding salt particles to the hot PVA solution does not form a hydrogel, but rather the composition remains a viscous emulsion solution (see col. 13, line 63-65). In order to form a hydrogel, Yao must freeze-thaw the solution. According to Yao, although the precursor solution is injected to a mold cavity, it does not form a hydrogel without the freeze-thaw treatment. In contrast, a hydrogel composition, according to the claimed invention, form a hydrogel from an injectable solution without freeze-thawing. As noted above, like Hyon and Ku, a freeze-thaw process does not permit preparation of an injectable formulation. Hence, Yao method can not yield an injectable hydrogel composition according to the claimed invention. Therefore, Yao does not anticipate the claimed invention.

Yamauchi *et al.* (JP 03215417) describe a hydrogel made of polyvinyl alcohol (PVA) containing salts of polysaccharides or hyaluronic acid. Yamauchi describes that the solution containing PVA and the salts is "...irradiated with ionized radiation to form a hydrogel". The hydrogel is then used for drug release. The salts are present to control

pore size, which aids in drug release rate. The salts are not used to form the hydrogel, however. Yamauchi explicitly states that the hydrogel is formed from covalently-bonded PVA through ionizing radiation. Moreover, the Yamauchi hydrogel formulation cannot be used in an "injectable" form, because a radiation source is required for the final gelation process. In contrast, the instant invention forms a hydrogel through physical cross-linking induced by the presence of the salt. Therefore, Yamauchi does not anticipate the claimed invention.

Okamura (JP 04338326A) describes a PVA-based hydrogel formulation to obtain a hydrogel sheet that contains NaCl, drug components, ethanol, urea, and face powder. The Okamura process also is the same freeze-thaw process disclosed by Hyon, Ku, and Yao, as described above. Additionally, the Okamura hydrogel also is not injectable. In contrast, the claimed the hydrogel is not frozen and is not formed into a sheet after the hydrogel has been created, and it is injectable. Hence, Okamura method can not yield an injectable hydrogel composition according to the claimed invention. Therefore, Okamura does not disclose the claimed invention. Okamura mentions that the NaCl "...contributes to the adjustment of the fresh feeling, transparency, and gel strength" (see Abstract). On the contrary, according to the instant invention, the NaCl decreases transparency through the formation of crystalline junction points, rather than increasing the transparency as it does in Okamura process. Therefore, Okamura disclosure does not anticipate the claimed invention.

Regarding the examiner's alleged obviousness rejection, applicants note that the examiner has failed to establish a *prima facie* case of obviousness and submit that:

"To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both

be found in the prior art, and not based on applicant's disclosure." MPEP 2142 (Rev. 4, October 2005), discussing *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Applicants also refer to the above discussion, analysis and arguments regarding each of the cited art and indicate that none of the cited art or any combination thereof teach or suggest all the claim limitations. Because the alleged obviousness rejection was based the examiner's belief that a generic disclosure of the claimed hydrogel is present in the cited arts. Applicants also point out that the claims relate to a injectable hydrogel composition, which is not in the generic disclosure of any of the cited references. Therefore, withdrawal of the obviousness rejection is solicited.

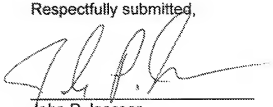
Finally, applicants submit that the claimed inventions are clearly distinguishable over all of the cited arts as none of the cited arts or any combination thereof disclose injectable hydrogel composition, or injectable hydrogel composition, which is substantially free of chemical crosslinkers.

Therefore, withdrawal of all alleged anticipation and obviousness rejections are earnestly requested.

REQUEST

Applicants submit that the claims 113-119 are in condition for allowance and respectfully request favorable consideration to that effect. The examiner is invited to contact the undersigned at (202) 416-6800 should there be any questions.

Respectfully submitted,



August 18, 2006
Date

John P. Isacson
Reg. No. 33,715

PROSKAUER ROSE LLP
1001 Pennsylvania Avenue, N.W.
Washington, D.C. 20004
Phone: 202-416-6800
Fax: 202-416-6899
Customer No. 61263